Advanced Synthesis & Catalysis

DOI: 10.1002/adsc.201301108

Diastereotopic Group Selection in Hydroxy-Directed Intramolecular C–H Alkenylation of Indole under Oxidative Palladium(II) Catalysis

Sandeep R. Kandukuri,[a,b] Lin-Yu Jiao,[a] Axel B. Machotta,[c] and Martin Oestreich[a,c,*]

[a] Institut für Chemie, Technische Universität Berlin, Strasse des 17. Juni 115, 10623 Berlin, Germany
Fax: (+49)-30-314-28829; e-mail: martin.oestreich@tu-berlin.de
[b] NRW Graduate School of Chemistry, Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstrasse 40, 48149 Münster, Germany
[c] Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstrasse 40, 48149 Münster, Germany

Received: December 9, 2013; Revised: February 5, 2014; Published online: ■■ ■■, 0000

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201301108.

Abstract: Group-selective palladium(II)-catalyzed ring closures involving C–H bond alkenylation are reported. The cyclization precursors contain a prochiral bis(homoallylic) alcohol unit tethered to either an arene or an indole. The homobenzylic hydroxy group in these substrates is positioned to act as a directing group in the *ortho*-selective C–H bond activation prior to the cyclization event. Arene-derived precursors reacted poorly, even when applying a protocol that had proven effective in intermolecular hydroxy-directed C–H bond alkenylations. No asymmetric induction was obtained with chiral ligands, mono-*N*-protected amino acids (MPAAs) in particular. Conversely, the cyclization of indole-derived precursors was substantially more efficient, and installation of a substituent in the benzylic position rendered these intramolecular C–H bond alkenylations diastereoselective. The diastereotopic group selection is high with diastereomeric ratios ranging from *dr* = 91:9 to 94:6.

Keywords: C–H bond activation; copper; cyclization; diastereoselectivity; palladium

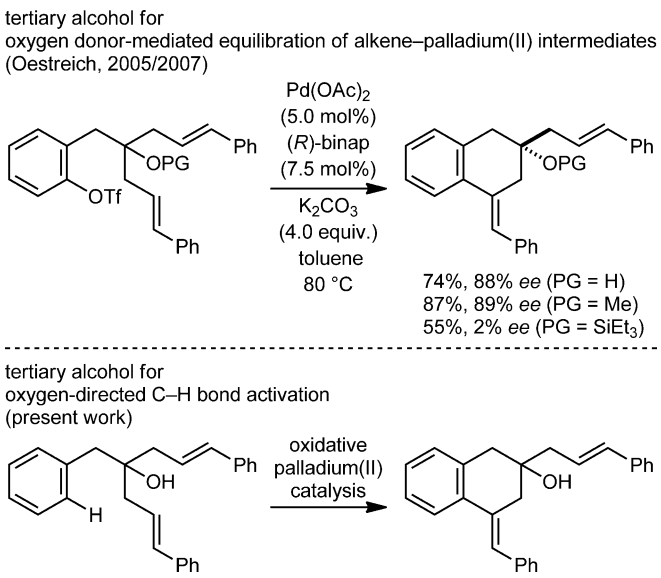
Introduction

The ability of an allylic hydroxy group to control the regioselectivity of intermolecular Heck alkenylation and arylation reactions is long known.[1,2] Aside from this established motif, a phenolic hydroxy group was found to be the pivotal structural element in a Heck macrocyclization.[3] A few years ago, our laboratory disclosed a unique desymmetrizing Heck cyclization where an oxygen donor equilibrates diastereomeric alkene-palladium(II) intermediates, thereby allowing for high enantioselection in the overall transformation (Scheme 1, *upper part*).[4] These examples illustrate the capability of an adequately positioned hydroxy group to interact with moderately oxophilic palladium(II) atoms. The hydroxy group therefore holds potential to act as a directing group in palladium(II)-catalyzed processes involving C–H bond activation. Recently, Yu and co-workers accomplished a hydroxy-directed C–H alkenylation of arenes.[5–7] The tertiary alcohol in that system is located relative to the C–H bond exactly as the C–X group in our prefunctionalized cyclization precursors (X = OTf). Hence, we reasoned that the same ring closure would occur under oxidative palladium(II) catalysis, perhaps even enantioselectively with Yu's mono-*N*-protected amino acids (MPAAs) as supporting ligands[8] (Scheme 1, *lower part*).

The new cyclization precursors for C–H bond activation would be derived from either benzene or C-3-substituted indole. Substitution in the benzylic position would add a stereocenter vicinal to the former prochiral carbon atom, and diastereotopic group-selective cyclizations[9] would then be possible (Figure 1).

Results and Discussion

As mentioned above, Yu and co-workers had developed a general methodology for the hydroxy-directed, intermolecular C–H alkenylation of arenes.[5] Howev-



Scheme 1. Different roles of a tertiary hydroxy group in palladium(0)- and palladium(II)-catalyzed intramolecular alkenylation.

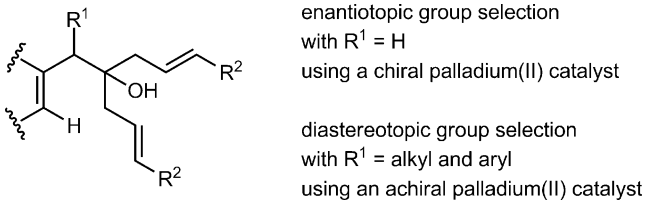
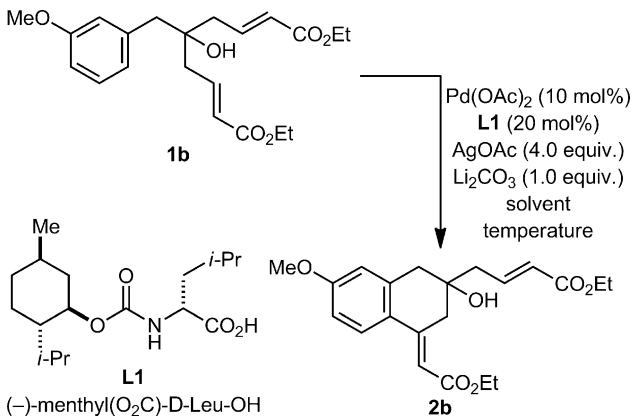


Figure 1. General structural motif for enantio- and diastereoselective cyclizations.

er, application of that protocol to the intramolecular desymmetrization outlined before failed (*cf.* Scheme 1, *lower part*). Conversion was moderate but the desired ring closure only occurred to a small extent, even with an OMe group *para* to the C–H bond. We then decided to replace the styrene units by α,β-unsaturated acceptors because the latter had also performed better in the intermolecular case.[5] The new precursor indeed cyclized at almost full conversion in promising yield under Yu's catalytic set-up with leucine-derived ligand **L1**[8] (**1b**→**2b**, Table 1, entry 1). Remarkably, the use of solvents other than C_6F_6 largely led to decomposition (Table 1, entries 2–7). 1,2-Dichloroethane (DCE) proved to be an exception, and **2b** was isolated in 42% yield (Table 1, entry 8). That yield did not improve any further in mixtures of C_6F_6 and DCE in various ratios. A brief survey of the terminal oxidant using C_6F_6 as solvent did not lead to any improvement, e.g., $Cu(OAc)_2$ (2.0 equiv.) or O_2 (ballon) afforded poor yields at less than 30% conversion. Also, isomerically pure **L1** and several related Yu-type ligands (not shown) did not induce any enantioselectivity within the experimental error. To illustrate these findings, we show three examples with more reactive acetylated ligands **L2**–**L4**[8f,g] (Figure 2).

Table 1. Solvent screening under Yu's catalytic set-up.[a]



Entry	Solvent	Temp. [°C]	Time [h]	Conv. [%][b]	Yield [%][b]
1	C_6F_6	90	64	90	35
2	toluene	110	64	67	9
3[c]	mesitylene	130	44	80	17
4	*n*-hexane	110	16	52	4
5	THF	110	16	30	0
6	*t*-AmOH	110	18	42	4
7	DMF	110	18	34	0
8	DCE	90	44	95	42[d]

[a] All reactions were conducted according to the General Procedure 1 in the indicated solvent and at the indicated temperature.
[b] Both conversion and yield were determined by GLC analysis using *n*-tetracosane as internal standard.
[c] $Pd(OAc)_2$ (1.0 equiv.) without oxidant.
[d] Isolated yield after flash column chromatography on silica gel.

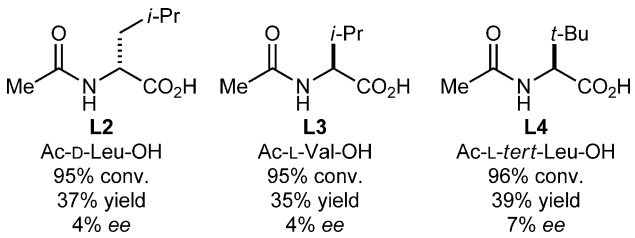
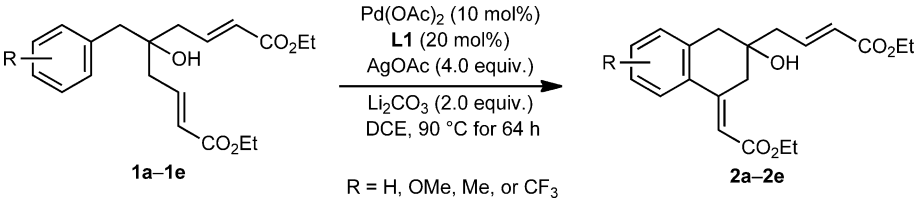
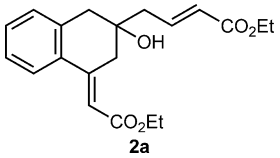
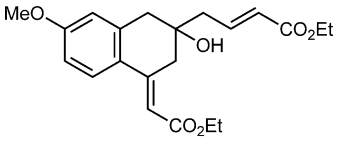
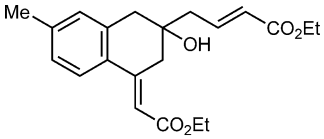
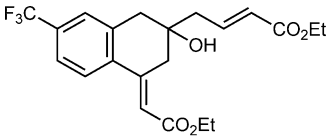
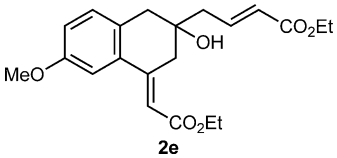


Figure 2. Performance of MPAAs **L2**–**L4** under optimized conditions (Table 1, entry 8).

We then tested a few representative cyclization precursors each with a different electronic situation at the arene ring (**1a**–**1e**, Table 2). Substrates **1a**–**1e** were accessed from the corresponding unsubstituted bis-(homoallylic) alcohols by two-directional cross-metathesis (see the Supporting Information for experimental details). The optimized protocol (Table 1) was slightly modified by doubling of the amount of Li_2CO_3 (2.0 equiv. instead of 1.0 equiv).[10] That minor

Table 2. Hydroxy-directed desymmetrizing C–H bond alkenylation of tethered arenes.[a]

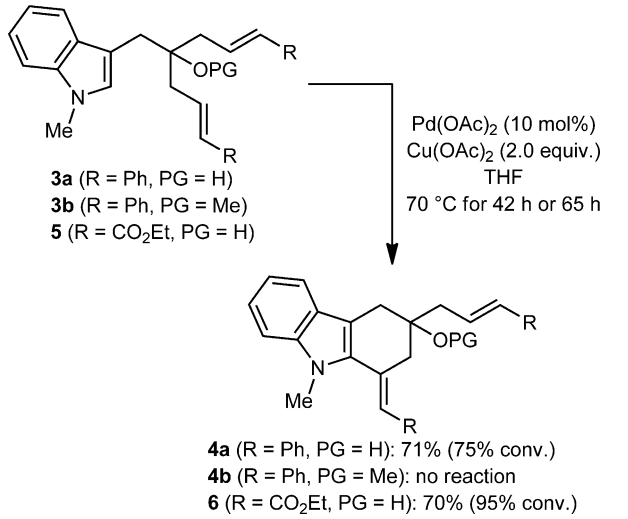


Entry	Arene	Annulated arene	Conv. [%][b]	Yield [%][c]
1	**1a**	 **2a**	92	20
2	**1b**	 **2b**	98	52
3	**1c**	 **2c**	92	32
4	**1d**	 **2d**	53	<5[d]
5	**1e**	 **2e**	90	10

[a] All reactions were conducted according to the General Procedure 1.
[b] Conversion was determined by GLC analysis by using *n*-tetracosane as internal standard.
[c] Isolated yield after flash column chromatography on silica gel.
[d] Determined by GLC analysis by using *n*-tetracosane as internal standard.

change further increased the yield of the model cyclization **1b**→**2b** (Table 2, entry 2). Yields were, however, substantially lower for the ring closures of the parent (unsubstituted) system and the precursor with an Me instead of an OMe group (**1a**→**2a** and **1c**→**2c**, Table 2, entries 1 and 3). The related electron-deficient arene with a CF_3 group did not cyclize at all (**1d**→**2d**, Table 2, entry 4). Shifting the position of the OMe group from *para* to *meta* relative to the C–H bond resulted in an unreactive precursor that decomposed quantitatively (**1e**→**2e**, Table 2, entry 5). The dramatic effect of the substitution pattern for the electron-rich arene was unexpected as Yu and coworkers had observed a less pronounced influence in the intermolecular hydroxy-directed C–H bond alkenylation (92% for *para* versus 71% yield for *meta*).[5]

The efficacy of the intramolecular desymmetrization of arenes **1a**–**1e** is poor, and it is essentially just a single precursor that cyclizes in reasonable yield but without any asymmetric induction. We, therefore, turned toward indoles tethered to bis(homoallylic) alcohols where the C–H bond activation is expected to be more facile.[11,12] We initially prepared indoles **3a** and **3b** substituted at the C-3 carbon atom. These would not undergo the desired ring closure under the previous catalytic set-ups. After considerable experimentation, we found out that the hydroxy- but not the methoxy-containing precursor[13] cyclizes cleanly in the absence of any added ligand with $Cu(OAc)_2$ as terminal oxidant to yield the annulated indole (**3a**→**4a** but not **3b**→**4b**, Scheme 2). That finding corroborates that the hydroxy group acts as a directing group.



Scheme 2. Desymmetrizing ring closures of indoles tethered to bis(homoallylic) alcohols.

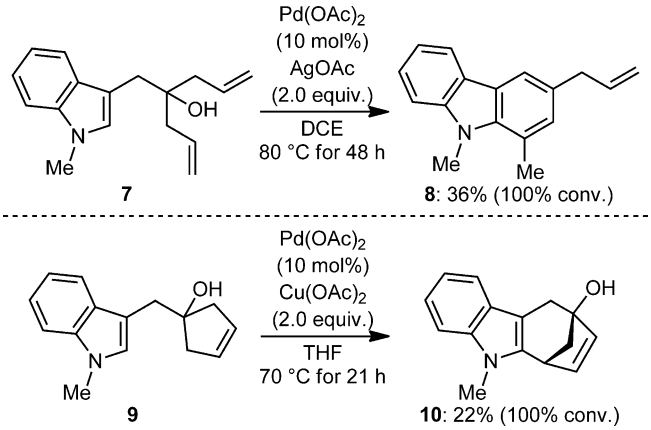
Also, the cognate substrate with the α,β-unsaturated acceptors afforded the new ring in good isolated yield (**5**→**6**, Scheme 2).

The terminally unsubstituted bis(homoallylic) unit also participated in the ring closure but *exo*-to-*endo* double bond migration and subsequent elimination of water resulted in aromatization of the newly formed ring (**7**→**8**, Scheme 3, *upper part*).[14] AgOAc was superior to $Cu(OAc)_2$ as terminal oxidant, and the carbazole was formed in 36% isolated yield. Cyclization of **9**, prepared from **7** by ring-closing metathesis, furnished the indole-annulated bicycle **10** in 22% isolated yield (**9**→**10**, Scheme 3, *lower part*).

The results obtained with the indole motif were encouraging (Scheme 2) but we were not able to develop an asymmetric procedure in the presence of a chiral ligand. Addition of ligands generally thwarted the C–H bond activation/cyclization sequence. That was particularly disappointing as we had accomplished enantioselective intramolecular C–H bond alkenylations of indoles and pyrroles under oxidative palladium(II) catalysis before.[15] An alternative approach to breaking the symmetry of the bis(homoallylic) alcohol fragment is by diastereotopic group selection.[9] That would require the installation of a substituent R^1 in the benzylic position of precursors **3** or **5** (**11**–**14**, Table 3). Diastereoselective cyclizations of alkenes with an additional stereocenter in the tether involving C–H bond alkenylation are rare though. Stoltz and co-workers had reported such ring closures yet diastereoselectivity was good in one case only: $dr = 50{:}50$ with an Me group in the benzylic and $dr = 85{:}15$ with an Me group in the homobenzylic position in a five-membered ring formation of an indole.[16]

We prepared six substrates **11**–**14** with different groups in the benzylic position and various alkyl esters. It turned out that the latter had a profound effect on conversion and isolated yield, increasing with the length of the alkyl chain (Bu > Et > Me, Table 3, entries 1–3). The diastereomeric ratio was not affected by the R^1 group. The cyclization of **11c** afforded *cis*-**15c** with good diastereoselectivity in excellent 81% yield. R^1 groups other than Me allowed for even higher diastereocontrol but *i*-Pr was already too bulky for the ring closure to occur (Table 3, entries 4–6). The relative configuration was assigned as *cis* by nOe measurements (see the Supporting Information for details).

The cyclic tertiary alcohols were prone to facile acid-mediated elimination, affording the corresponding carbazoles after aromatization. $CDCl_3$ with traces of acid was sufficient, and formation of the carbazole already occurred during NMR measurements. For example, *cis*-**15c** converted quantitatively into **19c** after one week in $CDCl_3$ at room temperature (Scheme 4). Neat samples of the tertiary alcohols were stable for extended periods of time. This finding was not totally unexpected as we had already seen carbazole formation with the parent bis(homoallylic) substrate (*cf.* **7**→**8**, Scheme 3, *upper part*).[14]

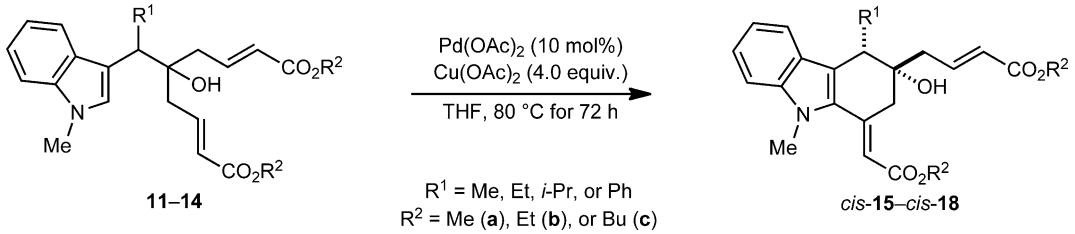


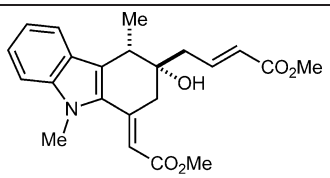
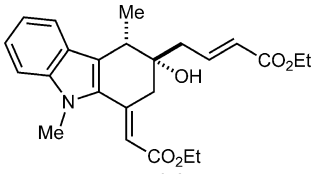
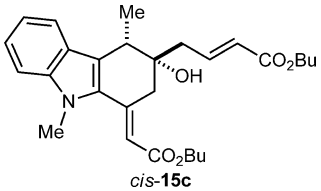
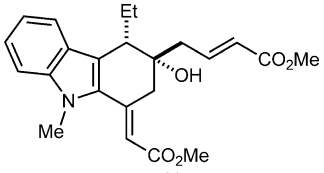
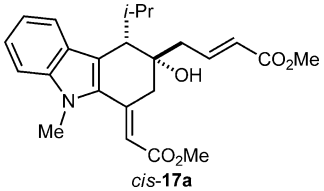
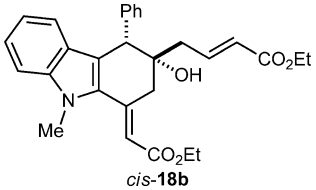
Scheme 3. Miscellaneous ring closures.

Conclusions

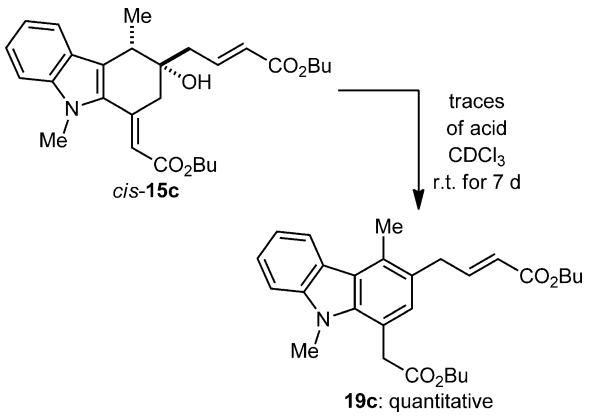
Our initial goal was to achieve enantiotopic group selection in a palladium(II)-catalyzed C–H alkenylation of bis(homoallylic) alcohols. The hydroxy group was believed to act as a directing group in the C–H bond activation step. We were, however, not able to identify a suitable chiral ligand, and ring closures occurred completely unselectively. In turn, the related diastereoselective variant where an existing stereocenter in the cyclization precursor controls the desymmetrization of the bis(homoallylic) alcohol unit proceeded with high levels of diastereoselection. An indole-derived substrate cyclized with $dr = 91{:}9$ in 81% isolated yield.

Table 3. Diastereotopic group selection in the intramolecular C–H bond alkenylation of indole.[a]



Entry	Indole	Annulated indole	Conv. [%][b]	Yield [%][c]	*dr*[d]
1	**11a**	 *cis*-**15a**	60	50[e]	92:8
2	**11b**	 *cis*-**15b**	87	68[e]	91:9
3	**11c**	 *cis*-**15c**	95	81	91:9
4	**12a**	 *cis*-**16a**	80	55	94:6
5	**13a**	 *cis*-**17a**	30	<10[f]	–[g]
6	**14b**	 *cis*-**18b**	62	30	94:6

[a] All reactions were conducted according to the General Procedure 2.
[b] Conversion was determined by GLC analysis by using *n*-tetracosane as internal standard.
[c] Isolated yield after flash column chromatography on silica gel.
[d] Diastereomeric ratio was determined by ^{1}H NMR spectroscopy prior to purification.
[e] Contaminated with traces of the cyclization precursor.
[f] Determined by GLC analysis by using *n*-tetracosane as internal standard.
[g] Not determined.



Scheme 4. Acid-mediated dehydration and aromatization.

Experimental Section

General Information

All reactions were performed in flame-dried glassware using conventional Schlenk techniques under a static pressure of nitrogen or argon. Liquids and solutions were transferred with syringes. Solvents were purified and dried following standard methods. Technical grade solvents for extraction and chromatography (cyclohexane, dichloromethane, ethyl acetate, *n*-pentane, diethyl ether, and *tert*-butyl methyl ether) were distilled prior to use. Hexafluorobenzene and 1,2-dichloroethane were dried over calcium hydride. Analytical thin-layer chromatography (TLC) was performed on silica gel 60 F_{254} glass plates from Merck. Flash column chromatography was performed on silica gel 60 (40–63 μm, 230–400 mesh, ASTM) by Merck or Grace GmbH using the indicated solvents. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on Bruker AV 400 and Bruker AV 500 instruments. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (TMS) and are referenced to the residual solvent resonance as the internal standard ($CHCl_3$: $\delta = 7.26$ ppm for ^{1}H and $CDCl_3$: $\delta = 77.16$ ppm for ^{13}C; DMSO: $\delta = 2.50$ ppm for ^{1}H and DMSO-d_6: $\delta = 39.52$ ppm for ^{13}C). Data are reported as follows: chemical shift, multiplicity (br s = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. Infrared (IR) spectra were recorded on an Agilent Technologies Cary 630 FT-IR spectrophotometer equipped with an ATR unit and are reported (br = broad; vw = very weak, w = weak, m = medium, s = strong) in wavenumbers (cm^{-1}). Gas liquid chromatography (GLC) was performed on an Agilent Technologies 7890 A gas chromatograph equipped with an HP-5 capillary column (30 m × 0.32 mm, 0.25 μm film thickness) by Agilent Technologies using the following program: N_2 carrier gas, injection temperature 250 °C, detector temperature 300 °C; temperature program: start temperature 40 °C, heating rate 10 °C·min^{-1}, end temperature 280 °C for 10 or 20 min. Enantiomeric excesses were determined by analytical high-performance liquid chromatography (HPLC) analysis on an Agilent Technologies 1200 Infinity instrument. Optical rotation was determined with a Polartronic H532 from Schmidt + Haensch; the analytes were measured as a solution in $CHCl_3$ in 1 dm cuvettes. Elemental analysis were carried out on a device of the type VarioEL from Elementaranalysensysteme GmbH in the Microanalytical Laboratory at the Organisch-Chemisches Institut of the Westfälische Wilhelms-Universität Münster or on a Flash 1112 from Thermo Fisher Scientific at the Institut für Chemie of the Technische Universität Berlin. Melting points (mp) were determined with a Stuart SMP20 apparatus and are not corrected. High resolution mass spectrometry (HR-MS) analyses were performed by the Analytical Facility at the Institut für Chemie of the Technische Universität Berlin.

General Procedure for the Hydroxy-Directed Intramolecular Palladium(II)-Catalyzed C−H Alkenylation Using AgOAc as Terminal Oxidant (GP1)

$Pd(OAc)_2$ (10 mol%), AgOAc (4.0 equiv.), Li_2CO_3 (2.0 equiv.), and (−)-menthyl(O_2C)-D-Leu-OH (**L1**; 20 mol%) were added to a flame-dried sealed Schlenk tube followed by the addition of a solution of the bis(homoallylic) alcohol (1.0 equiv.) in 1,2-dichloroethane (0.1 M). The reaction mixture was then heated at the indicated temperature and for the indicated time. The reaction was monitored by GLC analysis using tetracosane as internal standard. After cooling to room temperature, the reaction mixture was filtered through a pad of Celite®. The filtrate was concentrated under reduced pressure. Purification by flash column chromatography on silica gel using mixtures of cyclohexane and *tert*-butyl methyl ether as eluents afforded the analytically pure product.

General Procedure for the Hydroxy-Directed Intramolecular Palladium(II)-Catalyzed C−H Alkenylation Using $Cu(OAc)_2$ as Terminal Oxidant (GP2)

$Pd(OAc)_2$ (10 mol%), $Cu(OAc)_2$ (2.0–4.0 equiv.), and a solution of the bis(homoallylic) alcohol (1.0 equiv.) in dry THF (0.1 M) were added to a flame-dried sealed Schlenk tube. The reaction mixture was then heated at the indicated temperature and for the indicated time. The reaction was monitored by GLC or TLC analysis. After cooling to room temperature, the reaction mixture was diluted with ethyl acetate and filtered through a pad of Celite®. The filtrate was concentrated under reduced pressure, and (if applicable) the diastereomeric ratio was determined by ^{1}H NMR spectroscopy. Purification by flash column chromatography on silica gel using mixtures of cyclohexane and *tert*-butyl methyl ether or ethyl acetate as eluents afforded the analytically pure product.

Diethyl (2*E*,7*E*)-5-benzyl-5-hydroxynona-2,7-diendioate (1a, Table 2, entry 1): Prepared from 4-benzylhepta-1,6-dien-4-ol (**S2a**, 552 mg, 2.73 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (34 mg, 55 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 3:1) afforded the analytically pure product as a light brown oil; yield: 304 mg (32%). GLC (HP-5): $t_R = 26.2$ min; $R_f = 0.52$ (cyclohexane:*tert*-butyl methyl ether = 1:1); IR (ATR): $\tilde{\nu} = 3477$ (br), 3447 (br), 2981 (m), 2936 (m), 1699 (s), 1650 (s), 1267 (s), 1164 (s), 702 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta =$ 1.29 (t, $J = 7.1$ Hz, 6 H), 1.71 (br s, 1 H), 2.33 (dd, $J = 7.5$ Hz,

J=1.4 Hz, 4H), 2.80 (s, 2H), 4.20 (q, J=7.1 Hz, 4H), 5.90 (dt, J=15.6 Hz, J=1.3 Hz, 2H), 7.01 (dt, J=15.6 Hz, J=7.7 Hz, 2H), 7.18–7.23 (m, 2H), 7.26–7.36 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.4, 42.1, 45.9, 60.5, 73.9, 125.2, 127.2, 128.7, 130.7, 136.0, 143.6, 166.2; HR-MS (ESI): m/z=369.1677, calcd. exact mass for $[M+Na]^+$ ($C_{20}H_{26}O_5Na$): 369.1672; elemental analysis calcd. for $C_{20}H_{26}O_5$: C 69.34, H 7.56; found: C 69.49, H 7.23.

Diethyl (2*E*,7*E*)-5-hydroxy-5-(3-methoxybenzyl)nona-2,7-diendioate (1b, Table 2, entry 2): Prepared from 4-(3-methoxybenzyl)hepta-1,6-dien-4-ol (**S2b**, 501 mg, 2.78 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (27 mg, 44 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether=2.5:1) afforded the analytically pure product as a light brown oil; yield: 476 mg (58%). GLC (HP-5): t_R= 29.0 min; R_f=0.57 (cyclohexane:*tert*-butyl methyl ether= 1:2); IR (ATR): $\tilde{\nu}$=3482 (br), 2980 (br), 1711 (s), 1650 (s), 1260 (s), 1160 (s), 1038 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.29 (t, J=7.1 Hz, 6H), 1.78 (s, 1H), 2.33 (d, J= 7.5 Hz, 4H), 2.77 (s, 2H), 3.79 (s, 3H), 4.19 (q, J=7.1 Hz, 4H), 5.90 (dt, J=15.6 Hz, J=1.3 Hz, 2H), 6.73–6.84 (m, 3H), 7.01 (dt, J=15.6 Hz, J=7.5 Hz, 2H), 7.21–7.25 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.4, 42.2, 45.9, 55.3, 60.5, 73.8, 112.5, 116.4, 123.0, 125.2, 129.7, 137.5, 143.6, 159.8, 166.2; HR-MS (ESI): m/z=377.1958, calcd. exact mass for $[M+H]^+$ ($C_{21}H_{29}O_6$): 377.1959.

Diethyl (2*E*,7*E*)-5-hydroxy-5-(3-methylbenzyl)nona-2,7-diendioate (1c, Table 2, entry 3): Prepared from 4-(3-methylbenzyl)hepta-1,6-dien-4-ol (**S2c**, 503 mg, 2.33 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (29 mg, 46 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether=3:1) afforded the analytically pure product as a light brown oil; yield: 614 mg (73%). GLC (HP-5): t_R= 26.9 min; R_f=0.57 (cyclohexane:*tert*-butyl methyl ether= 1:1); IR (ATR): $\tilde{\nu}$=3486 (br), 2980 (m), 2934 (m), 1714 (s), 1650 (s), 1265 (s), 1162 (s), 1039 (s), 980 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.30 (t, J=7.2 Hz, 6H), 1.64 (br s, 1H), 2.33 (dd, J=7.8 Hz, J=1.4 Hz, 4H), 2.35 (s, 3H), 2.77 (s, 2H), 4.20 (q, J=7.1 Hz, 4H), 5.90 (dt, J=15.6 Hz, J= 1.4 Hz, 2H), 6.97–7.06 (m, 4H), 7.07–7.12 (m, 1H), 7.22–7.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.4, 21.5, 42.2, 45.8, 60.5, 73.8, 125.2, 127.7, 128.0, 128.7, 131.5, 135.9, 138.4, 143.7, 166.2; HR-MS (ESI): m/z=361.2018, calcd. exact mass for $[M+H]^+$ ($C_{21}H_{29}O_5$): 361.2010.

Diethyl (2*E*,7*E*)-5-hydroxy-5-[3-(trifluoromethyl)benzyl]-nona-2,7-diendioate (1d, Table 2, entry 4): Prepared from 4-[3-(trifluoromethyl)benzyl]hepta-1,6-dien-4-ol (**S2d**, 501 mg, 1.85 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (23 mg, 37 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane: *tert*-butyl methyl ether=3:1) afforded the analytically pure product as a light brown oil; yield: 650 mg (85%). GLC (HP-5): t_R=25.5 min; R_f=0.52 (cyclohexane:*tert*-butyl methyl ether=1:1); IR (ATR): $\tilde{\nu}$=3450 (br), 2983 (br), 2937 (m), 1699 (s), 1651 (s), 1327 (s), 1270 (m), 1160 (s), 1119 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.29 (t, J=7.1 Hz, 6H), 1.83 (br s, 1H), 2.32 (dd, J=7.5 Hz, J=1.2 Hz, 4H), 2.86 (s, 2H), 4.20 (q, J=7.1 Hz, 4H), 5.90 (d, J=15.7 Hz, 2H), 6.99 (dt, J=15.6 Hz, J=7.7 Hz, 2H), 7.40–7.47 (m, 2H), 7.49 (br s, 1H), 7.51–7.56 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.4, 42.2, 45.7, 60.6, 73.9, 123.9 (q, J=3.6 Hz), 124.0 (q, J=272.2 Hz), 125.6, 127.4 (q, J= 4.0 Hz), 128.9, 130.9 (q, J=32.3 Hz), 134.1, 137.3, 142.9, 166.1; ^{19}F NMR (471 MHz, $CDCl_3$): δ=−62.6 (s, 3F); HR-MS (ESI): m/z=453.1286, calcd. exact mass for $[M+K]^+$ ($C_{21}H_{25}F_3O_5K$): 453.1286; elemental analysis calcd. for $C_{21}H_{25}F_3O_5$: C 60.86, H 6.08; found: C 61.20, H 6.23.

Diethyl (2*E*,7*E*)-5-hydroxy-5-(4-methoxybenzyl)nona-2,7-diendioate (1e, Table 2, entry 5): Prepared from 4-(4-methoxybenzyl)hepta-1,6-dien-4-ol (**S2e**, 499 mg, 2.15 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (27 mg, 43 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether=3:1) afforded the analytically pure product as a light brown oil; yield: 493 mg (61%). GLC (HP-5): t_R= 29.5 min; R_f=0.56 (cyclohexane:*tert*-butyl methyl ether= 1:2); IR (ATR): $\tilde{\nu}$=3487 (br), 2981 (br), 2935 (m), 1713 (s), 1650 (s), 1510 (s), 1245 (s), 1163 (s), 1034 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.29 (t, J=7.1 Hz, 6H), 1.77 (br s, 1H), 2.31 (dd, J=7.4 Hz, J=1.3 Hz, 4H), 2.74 (s, 2H), 3.79 (s, 3H), 4.19 (q, J=7.2 Hz, 4H), 5.89 (d, J=15.6 Hz, 2H), 6.85 (d, J=8.6 Hz, 2H), 7.01 (dt, J=15.6 Hz, J=7.6 Hz, 2H), 7.12 (d, J=8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=14.4, 42.0, 44.9, 55.3, 60.5, 73.9, 114.1, 125.1, 127.9, 131.6, 143.7, 158.8, 166.2; HR-MS (ESI): m/z=399.1777, calcd. exact mass for $[M+Na]^+$ ($C_{21}H_{28}O_6Na$): 399.1778.

(1*E*,6*E*)-4-(*N*-Methyl-1*H*-indol-3-ylmethyl)-1,7-diphenylhepta-1,6-dien-4-ol (3a, Scheme 2): To a three-necked flask equipped with a reflux condenser, DIBAL-H (1.0 M in cyclohexane, 57.0 mL, 57.0 mmol, 15.0 equiv.), dry THF (60 mL), and diyne (**S7**, 1.54 g, 3.80 mmol, 1.00 equiv.) were added. The reaction mixture was heated to 68 °C for 3 days, and 2N NaOH (5 mL) was added at 0 °C. To the reaction mixture, *tert*-butyl methyl ether (150 mL) and 2N HCl (150 mL) were added. The organic phase was washed with saturated aqueous $NaHCO_3$ solution (80 mL) and dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether=6:1) afforded the analytically pure product as a light red oil; yield: 1.30 g (84%, E:Z≥99:1). The diastereomeric ratio was determined by ^{1}H NMR spectroscopy. R_f=0.34 (cyclohexane:-*tert*-butyl methyl ether=2:1); IR (ATR): $\tilde{\nu}$=3385 (br), 3026 (s), 2925 (s) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ=1.89 (br s, 1H), 2.50 (d, J=7.1 Hz, 4H), 3.02 (s, 2H), 3.79 (s, 3H), 6.37 (dt, J=15.8 Hz, J=7.0 Hz, 2H), 6.40 (d, J=15.9 Hz, 2H), 7.00 (s, 1H), 7.14 (ddd, J=8.0 Hz, J=7.0 Hz, J= 1.1 Hz, 1H), 7.21–7.27 (m, 3H), 7.30–7.39 (m, 9H), 7.66 (ddd, J=8.0 Hz, J=1.3 Hz, J=0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ=32.9, 35.5, 43.2, 74.9, 109.3, 109.4, 119.3, 119.7, 121.8, 126.1, 126.3, 127.3, 128.7, 128.7, 129.1, 133.5, 137.0, 137.7; HR-MS (ESI): m/z=430.2141, calcd. exact mass for $[M+Na]^+$ ($C_{29}H_{29}NONa$): 430.2141; elemental analysis calcd. for $C_{29}H_{29}NO$: C 85.47, H 7.17, N 3.44; found: C 85.07, H 7.25, N 3.05.

(1*E*,6*E*)-4-Methoxy-4-(1-methyl-1*H*-indol-3-ylmethyl)-1,7-diphenylhepta-1,6-diene (3b, Scheme 2): To a suspension of NaH (60% in mineral oil, 0.061 g, 1.5 mmol, 1.2 equiv.) in dry THF (2 mL) at 0 °C, a solution of tertiary alcohol **3a** (0.510 g, 1.27 mmol, 1.00 equiv.) in dry THF (4 mL) and methyl iodide (0.27 g, 1.9 mmol, 1.5 equiv.) were successively added dropwise. After 30 min, the ice bath was removed,

and vigorous stirring was continued at room temperature for 4 h. Then, saturated aqueous NH_4Cl (30 mL) was added at 0 °C. After 20 min, *tert*-butyl methyl ether (80 mL) was added, and the organic phase was washed with saturated aqueous $NaHCO_3$ solution (30 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 97:3) afforded the analytically pure product as a colorless oil; 0.509 g (95%). R_f = 0.67 (cyclohexane:*tert*-butyl methyl ether = 3:1); IR (ATR): $\tilde{\nu}$ = 3056 (m), 3026 (m), 2935 (s), 2825 (m) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 2.55 (ddd, J = 14.5 Hz, J = 7.1 Hz, J = 1.0 Hz, 2H), 2.56 (ddd, J = 14.6 Hz, J = 7.1 Hz, J = 1.0 Hz, 2H), 3.06 (s, 2H), 3.49 (s, 3H), 3.79 (s, 3H), 6.31–6.37 (m, 2H), 6.41 (d, J = 16.1 Hz, 2H), 7.09 (s, 1H), 7.14 (ddd, J = 7.8 Hz, J = 7.7 Hz, J = 0.6 Hz, 1H), 7.23–7.27 (m, 4H), 7.30–7.35 (m, 4H), 7.37 (d, J = 7.8 Hz, 4H), 7.63 (d, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 30.1, 32.8, 39.0, 49.5, 80.0, 109.2, 109.7, 118.9, 119.3, 121.4, 126.1, 126.2, 127.2, 128.2, 128.6, 129.1, 133.0, 136.6, 137.8; HR-MS (ESI): m/z = 444.2298, calcd. exact mass for $[M+Na]^+$ ($C_{30}H_{31}NONa$): 444.2298; elemental analysis calcd. for $C_{30}H_{31}NO$: C 85.47, H 7.41, N 3.32; found: C 85.60, H 7.32, N 2.93.

Diethyl (2*E*,7*E*)-5-(1-methyl-1*H*-indol-3-ylmethyl)-5-hydroxy-2,7-diendioate (5, Scheme 2): Prepared from cyclopentenol **9** (254 mg, 1.11 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (14 mg, 22 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 1:1) afforded the analytically pure product as a light brown oil; yield: 274 mg (62%). GLC (HP-5): t_R = 36.3 min; R_f = 0.40 (cyclohexane:*tert*-butyl methyl ether = 1:1); IR (ATR): $\tilde{\nu}$ = 3496 (br), 2930 (br), 1714 (s), 1651 (s), 1468 (m), 1368 (m), 1329 (w), 1266 (s), 1165 (s), 1041 (m), 981 (m), 739 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.2 Hz, 6H), 1.85 (s, 1H), 2.44 (d, J = 7.6 Hz, 4H), 2.94 (s, 2H), 3.79 (s, 3H), 4.20 (q, J = 7.1 Hz, 4H), 5.89 (dt, J = 15.6 Hz, J = 1.4 Hz, 1H), 6.95 (s, 1H), 7.05 (dt, J = 15.6 Hz, J = 7.6 Hz, 1H), 7.13 (ddd, J = 8.1 Hz, J = 7.5 Hz, J = 1.0 Hz, 1H), 7.24 (ddd, J = 8.0 Hz, J = 7.5 Hz, J = 1.1 Hz, 1H), 7.32 (ddd, J = 8.2 Hz, J = 1.2 Hz, J = 1.0 Hz, 1H), 7.59 (ddd, J = 7.9 Hz, J = 1.3 Hz, J = 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 33.0, 35.6, 42.2, 60.5, 74.1, 108.3, 109.5, 119.5, 119.6, 122.1, 124.9, 128.7, 128.8, 137.2, 144.1, 166.3; HR-MS (ESI): m/z = 422.1940, calcd. exact mass for $[M+Na]^+$ ($C_{23}H_{29}NO_5Na$): 422.1938.

4-(1-Methyl-1*H*-indol-3-ylmethyl)hepta-1,6-dien-4-ol (7, Scheme 3): Prepared from methyl 2-(1-methyl-1*H*-indol-3-yl)acetate (**S4**, 8.08 g, 39.7 mmol, 1.00 equiv.) and allylmagnesium bromide (0.740 M in Et_2O, 110 mL, 81.5 mmol, 2.05 equiv.) according to **GPS1**. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 3:1) afforded the analytically pure product as a pale yellow oil; yield: 10 g (98%). GLC (HP-5): t_R = 21.8 min; R_f = 0.50 (cyclohexane:*tert*-butyl methyl ether = 1:1); IR (ATR): $\tilde{\nu}$ = 3549 (br), 3072 (w), 2912 (w), 1638 (m), 1472 (s), 1374 (m), 1328 (m), 1157 (m), 1129 (m), 995 (m), 910 (m), 736 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.03 (br s, 1H), 2.33 (d, J = 7.3 Hz, 4H), 2.94 (s, 2H), 3.79 (s, 3H), 5.12–5.20 (m, 4H), 5.97 (ddt, J = 16.8 Hz, J = 10.2 Hz, J = 7.3 Hz, 2H), 6.98 (s, 1H), 7.15 (ddd, J = 8.4 Hz, J = 7.4 Hz, J = 0.9 Hz, 1H), 7.25 (ddd, J = 8.5 Hz, J = 7.5 Hz, J = 1.3 Hz, 1H), 7.33 (ddd, J = 8.3 Hz, J = 1.3 Hz, J = 0.9 Hz, 1H), 7.66 (ddd, J = 7.9 Hz, J = 1.1 Hz, J = 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.8, 35.0, 43.5, 73.8, 109.3, 109.4, 118.5, 119.2, 119.7, 121.7, 128.6, 129.1, 134.3, 137.0; HR-MS (ESI): m/z = 256.1698, calcd. exact mass for $[M+H]^+$ ($C_{17}H_{22}NO$): 256.1696.

1-[(1-Methyl-1*H*-indol-3-yl)methyl]cyclopent-3-enol (9, Scheme 3): Prepared from 4-(1-methyl-1*H*-indol-3-ylmethyl)-1,6-heptadien-4-ol (**7**, 500 mg, 1.96 mmol, 1.00 equiv.), and Grubbs II catalyst (34 mg, 0.039 mmol, 2.0 mol%) according to **GPS3**. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 3:1) afforded the analytically pure product as a light brown oil; yield: 280 mg (63%). GLC (HP-5): t_R = 21.2 min; R_f = 0.40 (cyclohexane:*tert*-butyl methyl ether = 1:1); IR (ATR): $\tilde{\nu}$ = 3418 (br), 3050 (m), 2906 (br), 1613 (m), 1545 (w), 1471 (s), 1423 (m), 1374 (m), 1327 (s), 1257 (m), 1126 (m), 949 (m), 886 (s), 735 (s), 666 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 2.00 (s, 1H), 2.37 (d, J = 15.5 Hz, 2H), 2.67 (d, J = 15.5 Hz, 2H), 3.12 (s, 2H), 3.79 (s, 3H), 5.72 (s, 1H), 7.00 (s, 1H), 7.15 (ddd, J = 8.3 Hz, J = 7.4 Hz, J = 0.9 Hz, 1H), 7.25 (ddd, J = 8.4 Hz, J = 7.6 Hz, J = 1.1 Hz, 1H), 7.33 (ddd, J = 8.2 Hz, J = 1.1 Hz, J = 0.9 Hz, 1H), 7.67 (ddd, J = 8.0 Hz, J = 1.2 Hz, J = 1.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.8, 36.5, 46.9, 81.6, 109.3, 110.6, 119.2, 119.5, 121.7, 128.1, 128.9, 128.9, 137.0; HR-MS (ESI): m/z = 228.1386, calcd. exact mass for $[M+H]^+$ ($C_{15}H_{18}NO$): 228.1383.

Dimethyl (2*E*,7*E*)-5-hydroxy-5-[1-(1-methyl-1*H*-indol-3-yl)ethyl]nona-2,7-dienedioate (11a, Table 3, entry 1): Prepared from 1-[1-(1-methyl-1*H*-indol-3-yl)ethyl]cyclopent-3-enol (**S16**, 100 mg, 0.410 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (5.8 mg, 8.2 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 3:1) afforded the analytically pure product as a light yellow oil; yield: 130 mg (82%). GLC (HP-5): t_R = 27.4 min; R_f = 0.26 (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu}$ = 3478 (br), 2946 (w), 1714 (s), 1651 (m), 1540 (w), 1460 (w), 1433 (m), 1328 (m), 1269 (s), 1168 (s), 1034 (m), 977 (m), 837 (s), 739 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 1.39 (d, J = 7.3 Hz, 3H), 1.80 (s, 1H), 2.35 (dd, J = 15.1 Hz, J = 7.9 Hz, 1H), 2.47 (ddd, J = 14.9 Hz, J = 7.4 Hz, J = 1.0 Hz, 1H), 2.51–2.56 (m, 2H), 3.26 (q, J = 7.4 Hz, 1H), 3.73 (s, 3H), 3.74 (s, 3H), 3.79 (s, 3H), 5.84 (d, J = 15.5 Hz, 1H), 5.91 (d, J = 15.5 Hz, 1H), 6.95 (s, 1H), 6.98–7.04 (m, 1H), 7.06–7.14 (m, 2H), 7.23 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.0 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 16.0, 33.0, 38.7, 39.3, 40.8, 51.6, 51.6, 76.3, 109.5, 114.8, 119.6, 119.9, 122.1, 123.9, 124.2, 127.7, 128.2, 137.0, 144.7, 145.0, 166.7, 166.7; HR-MS (APCI): m/z = 386.1960, calcd. exact mass for $[M+H]^+$ ($C_{22}H_{28}NO_5$): 386.1962.

Diethyl (2*E*,7*E*)-5-hydroxy-5-[1-(1-methyl-1*H*-indol-3-yl)-ethyl]nona-2,7-dienedioate (11b, Table 3, entry 2): Prepared from 1-[1-(1-methyl-1*H*-indol-3-yl)ethyl]cyclopent-3-enol (**S16**, 241 mg, 1.00 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (12.8 mg, 20.0 μmol, 2.00 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 4:1) afforded the analytically pure product as a yellow oil; yield: 360 mg (87%). GLC (HP-5): t_R = 29.1 min; R_f = 0.30 (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu}$ = 3552 (br), 2967 (w), 1709 (s), 1649

(s), 1541 (w), 1466 (m), 1367 (m), 1327 (m), 1265 (s), 1170 (s), 1038 (s), 978 (s), 843 (s), 738 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.29$ (t, $J = 7.2$ Hz, 6H), 1.39 (d, $J = 7.6$ Hz, 3H), 1.83 (br s, 1H), 2.35 (ddd, $J = 14.6$ Hz, $J = 7.7$ Hz, $J = 1.0$ Hz, 1H), 2.47 (ddd, $J = 14.8$ Hz, $J = 7.4$ Hz, $J = 1.5$ Hz, 1H), 2.51–2.56 (m, 2H), 3.26 (q, $J = 7.1$ Hz, 1H), 3.78 (s, 3H), 4.19 (q, $J = 7.2$ Hz, 2H), 4.19 (q, $J = 7.2$ Hz, 2H), 5.83 (dt, $J = 15.7$ Hz, $J = 1.3$ Hz, 1H), 5.90 (dd, $J = 15.7$ Hz, $J = 1.2$ Hz, 1H), 6.94 (s, 1H), 6.96–7.02 (m, 1H), 7.08 (d, $J = 7.9$ Hz, 1H), 7.13 (dd, $J = 7.9$ Hz, $J = 1.0$ Hz, 1H), 7.23 (ddd, $J = 7.2$ Hz, $J = 7.1$ Hz, $J = 1.0$ Hz, 1H), 7.31 (d, $J = 8.2$ Hz, 1H), 7.64 (d, $J = 8.1$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.3$, 14.4, 16.0, 32.9, 38.7, 39.2, 40.8, 60.3, 60.4, 76.3, 109.5, 114.8, 119.5, 119.9, 122.0, 124.3, 124.6, 127.6, 128.2, 137.0, 144.3, 144.7, 166.3, 166.3; HR-MS (APCI): $m/z = 414.2277$, calcd. exact mass for $[M+H]^+$ ($C_{24}H_{32}NO_5$): 414.2275.

Dibutyl (2*E*,7*E*)-5-hydroxy-5-[1-(1-methyl-1*H*-indol-3-yl)-ethyl]nona-2,7-dienedioate (11c, Table 3, entry 3): Prepared from 1-[1-(1-methyl-1*H*-indol-3-yl)ethyl]cyclopent-3-enol (**S16**, 100 mg, 0.410 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (5.8 mg, 8.2 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 5:1) afforded the analytically pure product as a yellow oil; yield: 150 mg (78%). GLC (HP-5): $t_R = 29.1$ min; $R_f = 0.45$ (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu} = 3495$ (br), 2956 (w), 1710 (s), 1649 (m), 1463 (m), 1372 (m), 1266 (s), 1167 (s), 1061 (m), 1027 (m), 977 (s), 840 (w), 737 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.95$ (t, $J = 7.4$ Hz, 3H), 0.95 (t, $J = 7.4$ Hz, 3H), 1.37–1.45 (m, 7H), 1.62–1.68 (m, 4H), 1.81 (br s, 1H), 2.35 (ddd, $J = 14.6$ Hz, $J = 7.7$ Hz, $J = 0.9$ Hz, 1H), 2.48 (ddd, $J = 14.8$ Hz, $J = 7.4$ Hz, $J = 1.3$ Hz, 1H), 2.51–2.59 (m, 2H), 3.27 (q, $J = 7.2$ Hz, 1H), 3.78 (s, 3H), 4.11–4.15 (m, 4H), 5.84 (d, $J = 15.8$ Hz, 1H), 5.91 (d, $J = 15.5$ Hz, 1H), 6.95 (s, 1H), 6.97–7.03 (m, 1H), 7.07 (dd, $J = 7.9$ Hz, $J = 7.8$ Hz, 1H), 7.12 (ddd, $J = 7.9$ Hz, $J = 7.9$ Hz, $J = 0.9$ Hz, 1H), 7.24 (ddd, $J = 7.0$ Hz, $J = 7.0$ Hz, $J = 0.8$ Hz, 1H), 7.31 (d, $J = 8.4$ Hz, 1H), 7.63 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 14.0$, 16.1, 19.4, 30.9, 33.0, 38.7, 39.3, 40.9, 64.4, 64.5, 76.4, 109.6, 115.0, 119.6, 120.0, 122.2, 124.5, 124.8, 127.7, 128.3, 137.1, 144.4, 144.7, 166.5, 166.5; HR-MS (APCI): $m/z = 470.2891$, calcd. exact mass for $[M+H]^+$ ($C_{28}H_{40}NO_5$): 470.2901.

Dimethyl (2*E*,7*E*)-5-hydroxy-5-[1-(1-methyl-1*H*-indol-3-yl)propyl]nona-2,7-dienedioate (12a, Table 3, entry 4): Prepared from 1-[1-(1-methyl-1*H*-indol-3-yl)propylcyclopent-3-enol (**S17**, 90 mg, 0.35 mmol, 1.0 equiv.) and Hoveyda–Grubbs II catalyst (4.4 mg, 7.0 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 3:1) afforded the analytically pure product as a light yellow oil; yield: 111 mg (80%). GLC (HP-5): $t_R = 33.8$ min; $R_f = 0.30$ (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu} = 3505$ (br), 2947 (w), 1707 (s), 1650 (m), 1432 (m), 1371 (w), 1327 (m), 1266 (s), 1165 (s), 1033 (m), 977 (m), 840 (w), 737 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.75$ (t, $J = 7.4$ Hz, 3H), 1.77–1.89 (m, 3H), 2.38 (dd, $J = 14.7$ Hz, $J = 8.2$ Hz, 1H), 2.47 (ddd, $J = 15.0$ Hz, $J = 7.4$ Hz, $J = 1.2$ Hz, 1H), 2.50–2.58 (m, 2H), 2.95 (dd, $J = 11.5$ Hz, $J = 3.5$ Hz, 1H), 3.73 (s, 3H), 3.74 (s, 3H), 3.79 (s, 3H), 5.83 (d, $J = 15.8$ Hz, 1H), 5.88 (d, $J = 15.8$ Hz, 1H), 6.92 (s, 1H), 6.98–7.04 (m, 1H), 7.07–7.14 (m, 2H), 7.24 (ddd, $J = 7.1$ Hz, $J = 7.1$ Hz, $J = 0.7$ Hz, 1H), 7.32 (d, $J = 8.2$ Hz, 1H), 7.62 (d, $J = 8.2$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 13.0$, 22.5, 33.0, 40.0, 40.7, 47.3, 51.6, 51.6, 76.5, 109.5, 112.0, 119.5, 120.0, 122.0, 123.8, 124.1, 128.1, 129.0, 137.3, 144.9, 145.2, 166.7, 166.7; HR-MS (APCI): $m/z = 400.2116$, calcd. exact mass for $[M+H]^+$ ($C_{23}H_{30}NO_5$): 400.2118.

Dimethyl (2*E*,7*E*)-5-hydroxy-5-[2-methyl-1-(1-methyl-1*H*-indol-3-yl)propyl]nona-2,7-dienedioate (13a, Table 3, entry 5): Prepared from 1-[2-methyl-1-(1-methyl-1*H*-indol-3-yl)propyl]cyclopent-3-enol (**S18**, 134 mg, 0.500 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (6.2 mg, 10 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 4:1→3:1) afforded the analytically pure product as a white solid; yield: 130 mg (63%); mp 156–157 °C. GLC (HP-5): $t_R = 34.5$ min; $R_f = 0.36$ (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu} = 3454$ (br), 2949 (w), 1696 (s), 1648 (m), 1438 (w), 1336 (w), 1267 (s), 1232 (m), 1193 (m), 1042 (m), 979 (s), 824 (w), 737 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 0.76$ (d, $J = 6.2$ Hz, 3H), 1.06 (d, $J = 6.2$ Hz, 3H), 1.85 (br s, 1H), 2.17–2.30 (m, 2H), 2.32–2.40 (m, 1H), 2.65–2.69 (m, 2H), 3.07 (s, 1H), 3.70 (s, 3H), 3.76 (s, 3H), 3.81 (s, 3H), 5.62 (d, $J = 15.6$ Hz, 1H), 5.95 (d, $J = 15.6$ Hz, 1H), 6.86–6.92 (m, 1H), 7.02–7.08 (m, 2H), 7.11 (ddd, $J = 7.2$ Hz, $J = 7.2$ Hz, $J = 0.7$ Hz, 1H), 7.22 (dd, $J = 7.2$ Hz, $J = 7.2$ Hz, 1H), 7.31 (d, $J = 8.2$ Hz, 1H), 7.53 (d, $J = 7.7$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 23.7$, 28.2, 33.0, 40.5, 42.2, 51.5, 51.7, 77.3, 109.2, 110.3, 119.2, 119.3, 121.8, 124.0, 124.4, 127.8, 136.4, 144.5, 166.7, 166.7; HR-MS (APCI): $m/z = 414.2267$, calcd. exact mass for $[M+H]^+$ ($C_{24}H_{32}NO_5$): 414.2275.

Diethyl (2*E*,7*E*)-5-hydroxy-5-[(1-methyl-1*H*-indol-3-yl)-(phenyl)methyl]nona-2,7-dienedioate (14b, Table 3, entry 6): Prepared from 1-[(1-methyl-1*H*-indol-3-yl)(phenyl)methyl]-cyclopent-3-enol (**S19**, 243 mg, 0.800 mmol, 1.00 equiv.) and Hoveyda–Grubbs II catalyst (10 mg, 16 μmol, 2.0 mol%) according to **GPS2**. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 4:1) afforded the analytically pure product as a brown oil; yield: 260 mg (68%). GLC (HP-5): $t_R = 32.2$ min; $R_f = 0.18$ (cyclohexane:ethyl acetate = 3:1); IR (ATR): $\tilde{\nu} = 3492$ (br), 2979 (w), 1699 (s), 1649 (m), 1470 (m), 1367 (m), 1326 (m), 1266 (s), 1217 (m), 1166 (s), 1094 (m), 1037 (s), 978 (s), 848 (w), 737 (s), 702 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.24$ (d, $J = 7.2$ Hz, 3H), 1.26 (d, $J = 7.2$ Hz, 3H), 2.03 (br s, 1H), 2.33–2.44 (m, 2H), 2.45–2.56 (m, 2H), 3.74 (s, 3H), 4.10–4.18 (m, 4H), 4.26 (s, 1H), 5.64 (d, $J = 15.7$ Hz, 1H), 5.72 (d, $J = 15.7$ Hz, 1H), 6.88–6.94 (m, 2H), 7.06 (ddd, $J = 8.0$ Hz, $J = 8.0$ Hz, $J = 1.0$ Hz, 1H), 7.14–7.18 (m, 2H), 7.22–7.26 (m, 3H), 7.31 (s, 1H), 7.49 (dd, $J = 8.3$ Hz, $J = 1.1$ Hz, 2H), 7.56 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 14.4$, 14.4, 33.0, 41.0, 41.1, 50.6, 60.4, 60.5, 76.8, 109.3, 113.6, 118.9, 119.3, 121.9, 124.8, 125.1, 126.9, 127.7, 128.3, 128.6, 129.6, 136.5, 141.2, 143.5, 143.7, 166.5; HR-MS (APCI): $m/z = 476.2436$, calcd. exact mass for $[M+H]^+$ ($C_{29}H_{34}NO_5$): 476.2431.

(*E*,*E*)-4-(2-Ethoxy-2-oxoethylidene)-2-(4-ethoxy-4-oxobut-2-enyl)-1,2,3,4-tetrahydro-2-naphthol (2a, Table 2, entry 1): Prepared from diethyl (2*E*,7*E*)-5-benzyl-5-hydroxynona-2,7-diendioate (**1a**, 69.3 mg, 0.200 mmol, 1.00 equiv.), $Pd(OAc)_2$ (4.5 mg, 20 μmol, 10 mol%), AgOAc (134 mg, 0.800 mmol, 4.00 equiv.), Li_2CO_3 (30 mg, 0.40 mmol, 2.0 equiv.), and **L1**

(12 mg, 40 μmol, 20 mol%) according to **GP1** at 90 °C for 64 h. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 1:2) afforded the analytically pure product as a light yellow oil; yield: 13.5 mg (20%). GLC (HP-5): t_R = 27.6 min; R_f = 0.5 (cyclohexane:*tert*-butyl methyl ether = 1:2); IR (ATR): $\tilde{\nu}$ = 3455 (br), 2920 (m), 1706 (s), 1619 (m), 1369 (m), 1269 (m), 1156 (s), 1042 (s), 985 (w), 864 (m), 764 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.2 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H), 1.75 (br s, 1H), 2.48 (ddd, J = 14.3 Hz, J = 7.5 Hz, J = 1.4 Hz, 1H), 2.54 (ddd, J = 14.0 Hz, J = 7.5 Hz, J = 1.4 Hz, 1H), 2.93 (d, J = 16.3 Hz, 1H), 2.97 (d, J = 16.3 Hz, 1H), 3.09 (dd, J = 16.4 Hz, J = 2.0 Hz, 1H), 3.57 (dd, J = 16.3 Hz, J = 1.5 Hz, 1H), 4.17–4.23 (m, 4H), 5.91 (ddd, J = 15.6 Hz, J = 1.6 Hz, J = 1.3 Hz, 1H), 6.47 (dd, J = 2.3 Hz, J = 1.6 Hz, 1H), 7.08 (m, 1H), 7.15 (dd, J = 7.5 Hz, J = 0.8 Hz, 1H), 7.22–7.26 (m, 1H), 7.32 (ddd, J = 8.2 Hz, J = 7.4 Hz, J = 1.2 Hz, 1H), 7.69 (dd, J = 8.0 Hz, J = 0.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.5, 40.0, 41.8, 44.3, 60.2, 60.5, 71.6, 115.3, 124.6, 125.4, 127.1, 130.3, 130.5, 133.1, 136.2, 143.4, 151.1, 166.2, 167.0; HR-MS (ESI): m/z = 367.1510, calcd. exact mass for $[M+Na]^+$ ($C_{20}H_{24}O_5Na$): 367.1516.

(*E*,*E*)-4-(2-Ethoxy-2-oxoethylidene)-2-(4-ethoxy-4-oxobut-2-enyl)-7-methoxy-1,2,3,4-tetrahydro-2-naphthol (2b, Table 1, entries 1–8 and Table 2, entry 2): Prepared from diethyl (2*E*,7*E*)-5-hydroxy-5-(3-methoxybenzyl)nona-2,7-dienedioate (**1b**, 27 mg, 0.071 mmol, 1.0 equiv.), $Pd(OAc)_2$ (1.6 mg, 7.1 μmol, 10 mol%), AgOAc (47.4 mg, 0.284 mmol, 4.00 equiv.), Li_2CO_3 (10.5 mg, 0.140 mmol, 2.00 equiv.), and **L1** (4.5 mg, 14 μmol, 20 mol%) according to **GP1** at 90 °C for 62 h. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 1:1) afforded the analytically pure product as a light brown oil; yield: 14 mg (52%). GLC (HP-5): t_R = 32.5 min; R_f = 0.35 (cyclohexane:*tert*-butyl methyl ether = 1:2); HPLC (Daicel Chiralpak AD-H column, column temperature 20 °C, solvent *n*-heptane:*i*-PrOH = 90:10, flow rate 0.70 mL·min^{-1}, λ = 230 nm): t_R = 62.3 min and t_R = 87.7 min; IR (ATR): $\tilde{\nu}$ = 3450 (br), 2980 (m), 2931 (m), 1700 (s), 1594 (s), 1498 (m), 1445 (w), 1368 (m), 1268 (m), 1235 (m), 1151 (s), 1039 (s), 984 (m), 832 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.28–1.34 (m, 6H), 1.73 (br s, 1H), 2.42 (dd, J = 14.1 Hz, J = 1.3 Hz, 1H), 2.60 (dd, J = 14.1 Hz, J = 1.4 Hz, 1H), 2.88 (d, J = 16.4 Hz, 1H), 2.97 (d, J = 16.4 Hz, 1H), 3.09 (dd, J = 16.5 Hz, J = 8.2 Hz, 1H), 3.56 (ddd, J = 16.5 Hz, J = 8.3 Hz, J = 1.5 Hz, 1H), 3.82 (s, 3H), 4.20 (m, 4H), 5.91 (ddd, J = 15.6 Hz, J = 1.3 Hz, J = 1.3 Hz, 1H), 6.36 (dd, J = 1.7 Hz, J = 1.7 Hz, 1H), 6.65 (d, J = 2.7 Hz, 1H), 6.80 (dd, J = 8.9 Hz, J = 2.7 Hz, 1H), 7.08 (ddd, J = 15.5 Hz, J = 7.7 Hz, J = 7.7 Hz, 1H), 7.65 (d, J = 8.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.4, 40.1, 42.0, 44.1, 55.4, 60.0, 60.5, 71.5, 112.8, 113.7, 114.2, 125.2, 125.6, 126.2, 138.2, 143.5, 151.0, 161.4, 166.2, 167.2; HR-MS (ESI): m/z = 375.1802, calcd. exact mass for $[M+H]^+$ ($C_{21}H_{27}O_6$): 375.1802.

(*E*,*E*)-4-(2-Ethoxy-2-oxoethylidene)-2-(4-ethoxy-4-oxobut-2-enyl)-7-methyl-1,2,3,4-tetrahydro-2-naphthol (2c, Table 2, entry 3): Prepared from diethyl (2*E*,7*E*)-5-hydroxy-5-(3-methylbenzyl)nona-2,7-dienedioate (**1c**, 72 mg, 0.20 mmol, 1.0 equiv.), $Pd(OAc)_2$ (4.5 mg, 20 μmol, 10 mol%), AgOAc (134 mg, 0.800 mmol, 4.00 equiv.), Li_2CO_3 (30 mg, 0.40 mmol, 2.0 equiv.), and **L1** (12 mg, 40 μmol, 20 mol%) according to **GP1** at 90 °C for 64 h. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 1:2) afforded the analytically pure product as a light yellow oil; yield: 22.6 mg (32%). GLC (HP-5): t_R = 29.0 min; R_f = 0.50 (cyclohexane:*tert*-butyl methyl ether = 1:2); IR (ATR): $\tilde{\nu}$ = 3470 (br), 2923 (s), 2853 (m), 1705 (s), 1604 (m), 1457 (m), 1368 (m), 1269 (m), 1154 (s), 1041 (m), 985 (w), 863 (w), 813 (m), 730 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.27–1.33 (m, 6H), 1.82 (br s, 1H), 2.32 (s, 3H), 2.46 (ddd, J = 14.0 Hz, J = 7.5 Hz, J = 1.4 Hz, 1H), 2.53 (ddd, J = 14.0 Hz, J = 7.5 Hz, J = 1.4 Hz, 1H), 2.87 (d, J = 16.3 Hz, 1H), 2.92 (d, J = 16.3 Hz, 1H), 3.10 (dd, J = 16.4 Hz, J = 1.8 Hz, 1H), 3.52 (dd, J = 16.5 Hz, J = 1.4 Hz, 1H), 4.16–4.22 (m, 4H), 5.89 (ddd, J = 15.6 Hz, J = 1.7 Hz, J = 1.2 Hz, 1H), 6.43 (dd, J = 2.4 Hz, J = 1.4 Hz, 1H), 6.96 (s, 1H), 7.03–7.12 (m, 2H), 7.59 (d, J = 8.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.5, 21.4, 40.1, 41.8, 44.1, 60.1, 60.5, 71.6, 114.2, 124.5, 125.3, 128.0, 130.2, 130.9, 136.1, 140.8, 143.5, 151.1, 166.2, 167.1; HR-MS (ESI): m/z = 381.1663, calcd. exact mass for $[M+Na]^+$ ($C_{21}H_{26}O_5Na$): 381.1672.

(*E*,*E*)-4-(2-Ethoxy-2-oxoethylidene)-2-(4-ethoxy-4-oxobut-2-enyl)-6-methoxy-1,2,3,4-tetrahydro-2-naphthol (2e, Table 2, entry 5): Prepared from diethyl (2*E*,7*E*)-5-hydroxy-5-(4-methoxybenzyl)nona-2,7-dienedioate (**1e**, 75.3 mg, 0.200 mmol, 1.00 equiv.), $Pd(OAc)_2$ (4.5 mg, 20 μmol, 10 mol%), AgOAc (134 mg, 0.800 mmol, 4.00 equiv.), Li_2CO_3 (30 mg, 0.40 mmol, 2.0 equiv.), and **L1** (12 mg, 40 μmol, 20 mol%) according to **GP1** at 90 °C for 64 h. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 1:2) afforded the analytically pure product as a light yellow oil; yield: 7.5 mg (10%). GLC (HP-5): t_R = 31.1 min; R_f = 0.40 (cyclohexane:*tert*-butyl methyl ether = 1:2); IR (ATR): $\tilde{\nu}$ = 3467 (br), 2979 (m), 1706 (s), 1619 (m), 1497 (m), 1430 (w), 1367 (m), 1271 (m), 1228 (w), 1151 (s), 1035 (s), 985 (m), 863 (m), 810 (m), 729 (m) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.29 (t, J = 7.2 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H), 1.70 (br s, 1H), 2.47 (ddd, J = 14.0 Hz, J = 7.5 Hz, J = 1.3 Hz, 1H), 2.54 (ddd, J = 14.0 Hz, J = 7.5 Hz, J = 1.4 Hz, 1H), 2.86 (d, J = 1.1 Hz, 1H), 2.90 (d, J = 16.1 Hz, 1H), 3.06 (dd, J = 16.3 Hz, J = 2.0 Hz, 1H), 3.53 (dd, J = 16.3 Hz, J = 1.2 Hz, 1H), 3.82 (s, 3H), 4.19 (q, J = 7.2 Hz, 2H), 4.21 (q, J = 7.1 Hz, 2H), 5.90 (ddd, J = 15.6 Hz, J = 1.2 Hz, J = 1.1 Hz, 1H), 6.43 (dd, J = 1.7 Hz, J = 1.6 Hz, 1H), 6.92 (dd, J = 8.4 Hz, J = 2.6 Hz, 1H), 7.04–7.12 (m, 2H), 7.17 (d, J = 2.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.5, 40.0, 41.1, 44.2, 55.6, 60.3, 60.5, 71.8, 108.8, 115.4, 117.4, 125.3, 128.4, 131.3, 133.9, 143.4, 151.1, 158.6, 166.2, 166.9; HR-MS (ESI): m/z = 397.1613, calcd. exact mass for $[M+Na]^+$ ($C_{21}H_{26}O_6Na$): 397.1622.

(*E*,*E*)-1-Benzylidene-9-methyl-3-(3-phenyl-2-propenyl)-1,2,3,4-tetrahydrocarbazol-3-ol (4a, Scheme 2): Prepared from (*E*,*E*)-4-(*N*-methyl-1*H*-indol-3-ylmethyl)-1,7-diphenylhepta-1,6-dien-4-ol (**3a**, 73.0 mg, 0.179 mmol, 1.00 equiv.), $Pd(OAc)_2$ (4.0 mg, 18 μmol, 10 mol%), and $Cu(OAc)_2$ (68.3 mg, 0.376 mmol, 2.10 equiv.) according to **GP2** at 70 °C for 65 h. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 6:1) afforded the analytically pure product as a light yellow oil (25% of starting material **3a** was recovered); yield: 51.5 mg (71%). R_f = 0.31 (cyclohexane:*tert*-butyl methyl ether = 3:1); IR (ATR): $\tilde{\nu}$ = 3548 (w), 2905 (br), 1597(m), 1493 (m), 1466

(m), 1447 (m), 1359 (s), 1072 (m), 738 (s), 694 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.07$ (br s, 1H), 2.40 (dd, $J = 13.7$ Hz, $J = 8.5$ Hz, 1H), 2.61 (dd, $J = 13.8$ Hz, $J = 6.8$ Hz, 1H), 2.96 (dd, $J = 13.6$ Hz, $J = 1.2$ Hz, 1H), 3.00 (dd, $J = 13.6$ Hz, $J = 1.2$ Hz, 1H), 3.04 (d, $J = 16.1$ Hz, 1H), 3.09 (d, $J = 16.1$ Hz, 1H), 3.95 (s, 3H), 6.13 (ddd, $J = 15.9$ Hz, $J = 8.4$ Hz, $J = 6.8$ Hz, 1H), 6.42 (d, $J = 15.9$ Hz, 1H), 7.03 (s, 1H), 7.13–7.15 (m, 3H), 7.18–7.35 (m, 7H), 7.39–7.41 (m, 3H), 7.53 (ddd, $J = 7.8$ Hz, $J = 1.2$ Hz, $J = 0.9$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 32.9$, 35.2, 40.6, 43.8, 73.8, 109.5, 112.4, 118.9, 119.6, 123.1, 125.2, 126.3, 126.8, 126.9, 126.9, 127.0, 127.3, 128.6, 128.6, 128.9, 129.4, 134.1, 134.4, 137.2, 140.3; HR-MS (ESI): $m/z = 428.1985$, calcd. exact mass for $[M+Na]^+$ ($C_{29}H_{27}NONa$): 428.1985.

(*E*,*E*)-1-(2-Ethoxy-2-oxoethylidene)-3-(4-ethoxy-4-oxobut-2-enyl)-9-methyl-1,2,3,4-tetrahydrocarbazol-3-ol (6, Scheme 2): Prepared from diethyl (2*E*,7*E*)-5-(1-methyl-1*H*-indol-3-ylmethyl)-5-hydroxy-2,7-diendioate (**5**, 30 mg, 0.075 mmol, 1.0 equiv.), $Pd(OAc)_2$ (1.7 mg, 7.5 μmol, 10 mol%), and $Cu(OAc)_2$ (54.6 mg, 0.300 mmol, 4.00 equiv.) according to **GP2** at 70 °C for 65 h. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 1:1) afforded the analytically pure product as a light yellow oil; yield: 21 mg (70%). GLC (HP-5): t_R = 41.5 min; $R_f = 0.47$ (cyclohexane:*tert*-butyl methyl ether = 1:2); IR (ATR): $\tilde{\nu} = 2923$ (br), 1637 (w), 1601 (m), 1463 (s), 1402 (m), 1300 (m), 1233 (s), 1136 (m), 1058 (w), 1098 (w), 993 (m), 909 (s), 768 (m), 744 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.30$ (t, $J = 7.2$ Hz, 3H), 1.33 (t, $J = 7.2$ Hz, 3H), 2.03 (br s, 1H), 2.56 (dd, $J = 14.2$ Hz, $J = 1.4$ Hz, 1H), 2.63 (dd, $J = 14.2$ Hz, $J = 1.4$ Hz, 1H), 3.03 (s, 2H), 3.12 (dd, $J = 15.0$ Hz, $J = 1.8$ Hz, 1H), 3.72 (d, $J = 15.0$ Hz, 1H), 3.89 (s, 3H), 4.17–4.25 (m, 4H), 5.93 (ddd, $J = 15.6$ Hz, $J = 1.7$ Hz, $J = 1.2$ Hz, 1H), 6.25 (s, 1H), 7.10–7.16 (m, 2H), 7.31–7.33 (m, 2H), 7.53 (ddd, $J = 8.0$ Hz, $J = 1.3$ Hz, $J = 1.0$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 14.4$, 14.5, 33.1, 34.6, 40.4, 44.1, 60.3, 60.5, 73.5, 109.9, 114.1, 117.1, 119.7, 120.1, 125.0, 125.3, 126.2, 132.5, 141.0, 143.6, 144.0, 166.3, 166.9; HR-MS (ESI): $m/z = 420.1770$, exact mass for $[M+Na]^+$ ($C_{23}H_{27}NO_5Na$): 420.1781.

1,9-Dimethyl-3-(prop-2-enyl)carbazole (8, Scheme 3): Prepared from 4-(1-methyl-1*H*-indol-3-ylmethyl)hepta-1,6-dien-4-ol (**7**, 51 mg, 0.20 mmol, 1.0 equiv.), $Pd(OAc)_2$ (4.5 mg, 20 μmol, 10 mol%), AgOAc (67 mg, 0.40 mmol, 2.0 equiv.) in 1,2-dichloroethane (2 mL) according to **GP1** at 80 °C for 48 h. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 49:1) afforded the analytically pure product as a pale yellow solid; yield: 18.2 g (36%); mp 62–64 °C. GLC (HP-5): t_R = 23.5 min; $R_f = 0.68$ (cyclohexane:*tert*-butyl methyl ether = 9:1); IR (ATR): $\tilde{\nu} = 2950$ (br), 2088 (br), 1635 (w), 1599 (m), 1463 (s), 1398 (m), 1347 (m), 1231 (m), 908 (s), 749 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.84$ (s, 3H), 3.52 (d, $J = 6.7$ Hz, 2H), 4.09 (s, 3H), 5.08 (ddt, $J = 10.0$ Hz, $J = 2.0$ Hz, $J = 0.4$ Hz, 1H), 5.23 (ddt, $J = 17.0$ Hz, $J = 2.0$ Hz, $J = 0.3$ Hz, 1H), 6.06 (ddt, $J = 17.0$ Hz, $J = 10.2$ Hz, $J = 6.7$ Hz, 1H), 7.01 (s, 1H), 7.19 (ddd, $J = 8.0$ Hz, $J = 7.5$ Hz, $J = 0.9$ Hz, 1H), 7.35 (d, $J = 8.5$ Hz, 1H), 7.44 (ddd, $J = 8.2$ Hz, $J = 7.7$ Hz, $J = 1.1$ Hz, 1H), 7.75 (s, 1H), 8.03 (ddd, $J = 7.8$ Hz, $J = 1.2$ Hz, $J = 0.9$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 20.4$, 32.4, 40.2, 108.6, 115.3, 117.9, 118.8, 120.1, 120.4, 122.9, 123.9, 125.6, 129.9, 130.8, 138.5, 138.7, 142.1; HR-MS (ESI): $m/z = 236.1433$, calcd. exact mass for $[M+H]^+$ ($C_{17}H_{18}N$): 236.1434.

5-Methyl-5,6,9,10-tetrahydro-6,9-methanocyclohepta[*b*]indol-9-ol (10, Scheme 3): Prepared from 1-[(1-methyl-1*H*-indol-3-yl)methyl]cyclopent-3-enol (**9**, 37 mg, 0.16 mmol, 1.0 equiv.), $Pd(OAc)_2$ (3.70 mg, 16.2 μmol, 10.0 mol%), and $Cu(OAc)_2$ (63 mg, 0.34 mmol, 2.1 equiv.) according to **GP2** at 70 °C for 21 h. Purification by flash column chromatography on silica gel (cyclohexane:*tert*-butyl methyl ether = 1:1) afforded the analytically pure product as a light yellow oil; yield: 8.0 mg (22%). GLC (HP-5): t_R = 22.1 min; $R_f = 0.40$ (cyclohexane:*tert*-butyl methyl ether = 1:1); IR (ATR): $\tilde{\nu} = 3459$ (br), 2979 (br), 1703 (s), 1601 (s), 1466 (m), 1367 (m), 1266 (m), 1230 (m), 1153 (s), 1043 (m), 850 (m), 805 (w), 740 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 2.00$ (s, 1H), 2.18 (d, $J = 9.2$ Hz, 1H), 2.29 (dd, $J = 9.1$ Hz, $J = 5.0$ Hz, 1H), 2.94 (d, $J = 15.2$ Hz, 1H), 3.06 (d, $J = 15.2$ Hz, 1H), 3.70 (s, 3H), 3.73 (dd, $J = 4.7$ Hz, $J = 4.8$ Hz, 1H), 5.74 (d, $J = 5.6$ Hz, 1H), 6.27 (dd, $J = 5.6$ Hz, $J = 5.5$ Hz, 1H), 7.06 (ddd, $J = 8.3$ Hz, $J = 7.6$ Hz, $J = 1.0$ Hz, 1H), 7.13 (ddd, $J = 8.0$ Hz, $J = 7.7$ Hz, $J = 1.2$ Hz, 1H), 7.24 (ddd, $J = 8.1$ Hz, $J = 1.1$ Hz, $J = 0.9$ Hz, 1H), 7.43 (ddd, $J = 7.8$ Hz, $J = 1.2$ Hz, $J = 1.0$ Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 29.4$, 33.0, 38.1, 51.5, 83.0, 106.2, 109.2, 117.5, 119.3, 120.5, 127.5, 135.7, 136.6, 137.8, 140.6; HR-MS (ESI): $m/z = 226.1227$, calcd. exact mass for $[M+H]^+$ ($C_{15}H_{16}NO$): 226.1226.

Methyl *cis*-(*E*,*E*)-4-[3-hydroxy-1-(2-methoxy-2-oxoethylidene)-4,9-dimethyl-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl]but-2-enoate (*cis*-15a, Table 3, entry 1): Prepared from dimethyl (2*E*,7*E*)-5-hydroxy-5-[1-(1-methyl-1*H*-indol-3-yl)ethyl]nona-2,7-dienedioate (**11a**, 39 mg, 0.10 mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.3 mg, 10 μmol, 10 mol%), and $Cu(OAc)_2$ (74 mg, 0.40 mmol, 4.0 equiv.) in THF (1.0 mL) according to **GP2** at 80 °C for 72 h. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 3:1) afforded the analytically pure product as a light brown oil; yield: 19 mg (50%). GLC (HP-5): t_R = 37.2 min; $R_f = 0.25$ (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu} = 3545$ (br), 2948 (w), 1704 (s), 1651 (m), 1465 (m), 1265 (s), 1033 (m), 978 (s), 839 (w), 734 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): $\delta = 1.38$ (d, $J = 7.0$ Hz, 3H), 2.10 (br s, 1H), 2.39–2.44 (m, 1H), 2.51–2.55 (m, 1H), 3.00 (dd, $J = 14.7$ Hz, $J = 1.8$ Hz, 1H), 3.29 (q, $J = 7.6$ Hz, 1H), 3.72 (s, 3H), 3.77 (s, 3H), 3.79 (d, $J = 14.9$ Hz, 1H), 3.87 (s, 3H), 5.76 (d, $J = 16.0$ Hz, 1H), 6.20 (d, $J = 1.2$ Hz, 1H), 7.08 (dd, $J = 7.0$ Hz, $J = 1.8$ Hz, 1H), 7.11–7.15 (m, 1H), 7.31–7.34 (m, 2H), 7.59 (d, $J = 7.9$ Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): $\delta = 15.9$, 33.1, 36.3, 37.2, 42.1, 51.4, 52.4, 75.3, 110.0, 112.9, 119.2, 119.9, 120.1, 123.0, 124.8, 124.9, 125.4, 131.8, 141.2, 144.4, 166.6, 167.1; HR-MS (APCI): $m/z = 384.1813$, calcd. exact mass for $[M+H]^+$ ($C_{22}H_{26}NO_5$): 384.1805.

Ethyl *cis*-(*E*,*E*)-4-[1-(2-ethoxy-2-oxoethylidene)-3-hydroxy-4,9-dimethyl-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl]but-2-enoate (*cis*-15b, Table 3, entry 2): Prepared from diethyl (2*E*,7*E*)-5-hydroxy-5-[1-(1-methyl-1*H*-indol-3-yl)ethyl]nona-2,7-dienedioate (**11b**, 41 mg, 0.10 mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.3 mg, 10 μmol, 10 mol%), and $Cu(OAc)_2$ (74 mg, 0.40 mmol, 4.0 equiv.) in THF (1.0 mL) according to **GP2** at 80 °C for 72 h. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 4:1) afforded the analytically pure product as a light brown oil; yield: 28 mg (68%). GLC (HP-5): t_R = 30.9 min; $R_f = 0.35$

(cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu}$ = 3457 (br), 2973 (w), 2924 (w), 1701 (s), 1595 (s), 1461 (m), 1364 (m), 1340 (m), 1263 (m), 1225 (m), 1151 (s), 1035 (s), 972 (m), 853 (m), 739 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.2 Hz, 3H), 1.34 (t, J = 7.2 Hz, 3H), 1.39 (d, J = 7.2 Hz, 3H), 2.14 (br s, 1H), 2.42 (dd, J = 14.5 Hz, J = 7.8 Hz, 1H), 2.54 (ddd, J = 14.5 Hz, J = 8.0 Hz, J = 1.2 Hz, 1H), 3.03 (d, J = 14.7 Hz, 1H), 3.29 (q, J = 7.0 Hz, 1H), 3.78 (d, J = 14.7 Hz, 1H), 3.88 (s, 3H), 4.17 (q, J = 7.2 Hz, 2H), 4.23 (dq, J = 7.0 Hz, J = 1.6 Hz, 2H), 5.76 (d, J = 15.5 Hz, 1H), 6.20 (s, 1H), 7.09 (dd, J = 15.7 Hz, J = 7.7 Hz, 1H), 7.11–7.15 (m, 1H), 7.31–7.34 (m, 2H), 7.60 (d, J = 7.9 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.4, 14.5, 15.9, 33.2, 36.4, 37.2, 42.2, 60.3, 60.4, 75.3, 110.1, 113.4, 120.0, 120.1, 124.2, 124.8, 125.1, 125.7, 131.7, 141.2, 143.9, 144.3, 166.2, 166.8; HR-MS (APCI):
m/z = 412.2115, calcd. exact mass for $[M+H]^+$ ($C_{24}H_{30}NO_5$): 412.2118.

Butyl *cis*-(*E*,*E*)-4-[1-(2-butoxy-2-oxoethylidene)-3-hydroxy-4,9-dimethyl-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl]but-2-enoate (*cis*-15c, Table 3, entry 3): Prepared from dibutyl (2*E*,7*E*)-5-hydroxy-5-[1-(1-methyl-1*H*-indol-3-yl)ethyl]nona-2,7-dienedioate (**11c**, 47 mg, 0.10 mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.3 mg, 10 μmol, 10 mol%), and $Cu(OAc)_2$ (74 mg, 0.40 mmol, 4.0 equiv.) in THF (1.0 mL) according to **GP2** at 80 °C for 72 h. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 6:1) afforded the analytically pure product as a brown oil; yield: 38 mg (81%). GLC (HP-5): t_R = 37.5 min; R_f = 0.55 (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu}$ = 3499 (br), 2955 (w), 1705 (s), 1652 (m), 1461 (m), 1370 (m), 1258 (s), 1166 (s), 1062 (m), 1028 (m), 988 (s), 839 (w), 737 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 0.94 (t, J = 7.2 Hz, 3H), 0.91 (t, J = 7.2 Hz, 3H), 1.38 (d, J = 7.2 Hz, 3H), 1.39–1.47 (m, 4H), 1.61–1.71 (m, 4H), 2.42 (dd, J = 14.5 Hz, J = 7.2 Hz, 1H), 2.53 (ddd, J = 14.5 Hz, J = 7.9 Hz, J = 1.1 Hz, 1H), 3.04 (dd, J = 14.9 Hz, J = 1.8 Hz, 1H), 3.29 (q, J = 7.0 Hz, 1H), 3.79 (d, J = 14.9 Hz, 1H), 3.88 (s, 3H), 4.11 (t, J = 6.6 Hz, 2H), 4.17 (t, J = 6.6 Hz, 2H), 5.76 (dt, J = 15.6 Hz, J = 1.7 Hz, 1H), 6.20 (d, J = 1.4 Hz, 1H), 7.08 (dd, J = 15.6 Hz, J = 7.7 Hz, 1H), 7.11–7.16 (m, 1H), 7.31–7.34 (m, 2H), 7.60 (d, J = 8.1 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.9, 13.9, 15.9, 19.4, 29.8, 30.8, 30.9, 33.2, 36.6, 37.1, 42.2, 64.3, 64.3, 75.3, 110.0, 113.4, 120.0, 120.1, 124.2, 124.8, 125.1, 125.7, 131.7, 141.2, 143.9, 144.3, 166.3, 166.9; HR-MS (APCI):
m/z = 468.2748, calcd. exact mass for $[M+H]^+$ ($C_{28}H_{38}NO_5$): 468.2744.

Methyl *cis*-(*E*,*E*)-4-[4-ethyl-3-hydroxy-1-(2-methoxy-2-oxoethylidene)-9-methyl-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl]but-2-enoate (*cis*-16a, Table 3, entry 4): Prepared from dimethyl (2*E*,7*E*)-5-hydroxy-5-[1-(1-methyl-1*H*-indol-3-yl)propyl]nona-2,7-dienedioate (**12a**, 40 mg, 0.10 mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.3 mg, 10 μmol, 10 mol%), and $Cu(OAc)_2$ (74 mg, 0.40 mmol, 4.0 equiv.) in THF (1.0 mL) according to **GP2** at 80 °C for 72 h. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 4:1) afforded the analytically pure product as a light brown oil; yield: 22 mg (55%). GLC (HP-5): t_R = 37.5 min; R_f = 0.30 (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu}$ = 3502 (br), 2949 (w), 1702 (s), 1648 (m), 1430 (m), 1369 (w), 1325 (m), 1260 (s), 1163 (s), 1030 (m), 978 (m), 838 (w), 737 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.01 (t, J = 7.3 Hz, 3H), 1.44–1.51 (m, 1H), 1.90 (br s, 1H), 2.13–2.19 (m, 1H), 2.32–2.41 (m, 2H), 3.01 (dd, J = 8.8 Hz, J = 4.6 Hz, 1H), 3.06 (dd, J = 15.6 Hz, J = 2.1 Hz, 1H), 3.70 (s, 3H), 3.74 (d, J = 4.7 Hz, 1H), 3.76 (s, 3H), 3.89 (s, 3H), 5.65 (d, J = 15.5 Hz, 1H), 6.19 (d, J = 0.9 Hz, 1H), 6.98–7.05 (m, 1H), 7.13 (ddd, J = 7.1 Hz, J = 7.1 Hz, J = 0.7 Hz, 1H), 7.31–7.34 (m, 2H), 7.57 (d, J = 7.7 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.7, 24.7, 33.4, 37.6, 43.0, 44.3, 51.4, 51.5, 75.6, 109.9, 112.0, 120.1, 120.6, 124.4, 124.6, 125.0, 126.7, 131.6, 141.1, 144.4, 144.6, 166.6, 167.2; HR-MS (APCI): m/z = 398.1967, calcd. exact mass for $[M+H]^+$ ($C_{23}H_{28}NO_5$): 398.1962.

Ethyl *cis*-(*E*,*E*)-4-[1-(2-ethoxy-2-oxoethylidene)-3-hydroxy-9-methyl-4-phenyl-2,3,4,9-tetrahydro-1*H*-carbazol-3-yl]but-2-enoate (*cis*-18b, Table 3, entry 6): Prepared from diethyl (2*E*,7*E*)-5-hydroxy-5-[(1-methyl-1*H*-indol-3-yl)-(phenyl)methyl]nona-2,7-dienedioate (**14b**, 47 mg, 0.10 mmol, 1.0 equiv.), $Pd(OAc)_2$ (2.3 mg, 10 μmol, 10 mol%), and $Cu(OAc)_2$ (74 mg, 0.40 mmol, 4.0 equiv.) in THF (1.0 mL) according to **GP2** at 80 °C for 72 h. Purification by flash column chromatography on silica gel (cyclohexane:ethyl acetate = 3:1) afforded the analytically pure product as a light brown oil; yield: 14 mg (30%). GLC (HP-5): t_R = 34.0 min; R_f = 0.25 (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu}$ = 2918 (m), 2849 (m), 1713 (s), 1596 (m), 1461 (m), 1339 (m), 1258 (s), 1165 (m), 1092 (m), 1022 (s), 797 (s), 745 (s), 699 (s) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.28 (t, J = 7.4 Hz, 3H), 1.34 (t, J = 7.4 Hz, 3H), 1.63 (br s, 1H), 2.52 (dd, J = 14.9 Hz, J = 7.2 Hz, 1H), 2.60 (dd, J = 14.9 Hz, J = 8.1 Hz, 1H), 3.34 (dd, J = 14.9 Hz, J = 0.9 Hz, 1H), 3.45 (d, J = 14.9 Hz, 1H), 3.96 (s, 3H), 4.18 (q, J = 7.0 Hz, 2H), 4.23 (q, J = 7.0 Hz, 2H), 4.42 (s, 1H), 5.83 (d, J = 15.6 Hz, 1H), 6.23 (d, J = 1.3 Hz, 1H), 6.87–6.92 (m, 2H), 7.13 (dd, J = 7.8 Hz, J = 7.8 Hz, 1H), 7.17–7.21 (m, 3H), 7.28–7.32 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.4, 14.5, 29.8, 31.1, 35.3, 37.7, 42.6, 61.4, 74.6, 108.4, 114.4, 120.0, 121.8, 122.3, 124.7, 124.9, 125.8, 127.8, 129.0, 129.5, 130.4, 131.2, 138.2, 144.1, 148.9, 166.7, 166.8; HR-MS (APCI); m/z = 474.2278, calcd. exact mass for $[M+H]^+$ ($C_{29}H_{32}NO_5$): 474.2275.

Butyl (*E*)-4-[1-(2-butoxy-2-oxoethyl)-4,9-dimethyl-9*H*-carbazol-3-yl]but-2-enoate (19c, Scheme 4): GLC (HP-5): Yellow solid; yield: quantative; mp 89–91 °C. t_R = 39.8 min; R_f = 0.55 (cyclohexane:ethyl acetate = 2:1); IR (ATR): $\tilde{\nu}$ = 2955 (w), 2870 (w), 1713 (s), 1648 (m), 1578 (w), 1465 (m), 1377 (w), 1321 (m), 1265 (s), 1156 (s), 1120 (m), 1062 (m), 1023 (m), 983 (m), 730 (s) cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 0.91 (t, J = 7.3 Hz, 3H), 0.94 (t, J = 7.3 Hz, 3H), 1.31–1.42 (m, 4H), 1.59–1.66 (m, 4H), 2.80 (s, 3H), 3.74 (dd, J = 6.1 Hz, J = 1.3 Hz, 2H), 4.10 (s, 3H), 4.13 (t, J = 6.7 Hz, 2H), 4.14 (d, J = 7.3 Hz, 2H), 4.15 (s, 2H), 5.70 (dt, J = 15.6 Hz, J = 1.9 Hz, 1H), 7.08 (s, 1H), 7.22 (dt, J = 15.6 Hz, J = 6.4 Hz, 1H), 7.28 (dd, J = 6.7 Hz, J = 0.6 Hz, 1H), 7.44 (d, J = 8.3 Hz, 1H), 7.51 (dd, J = 8.3 Hz, J = 7.9 Hz, 1H), 8.27 (d, J = 8.0 Hz, 1H); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 13.7, 13.8, 16.7, 19.2, 19.3, 30.7, 30.8, 32.1, 36.0, 39.0, 64.2, 65.1, 108.5, 114.2, 119.1, 121.9, 122.9, 123.5, 123.7, 125.3, 126.4, 131.2, 131.9, 138.7, 142.2, 148.1, 166.9, 172.2; HR-MS (APCI): m/z = 450.2645, calcd. exact mass for $[M+H]^+$ ($C_{28}H_{36}NO_4$): 450.2639.

Acknowledgements

S.R.K. and L.-Y.J. thank the NRW Graduate School of Chemistry and the China Scholarship Council (CSC), respectively for predoctoral fellowships (2009–2012 and 2011–2015, respectively). M.O. is indebted to the Einstein Foundation (Berlin) for an endowed professorship. We thank Dr. Sebastian Kemper (TU Berlin) for expert advice with the NMR measurements and we are grateful to Felix Pape (TU Berlin) for his experimental contributions.

References

[1] For reviews on directed Mizoroki–Heck reactions, see: a) M. Oestreich, *Eur. J. Org. Chem.* **2005**, 783–792; b) M. Oestreich, *Top. Organomet. Chem.* **2007**, *24*, 169–192; c) K. Itami, J.-i. Yoshida, in: *The Mizoroki–Heck Reaction*, (Ed.: M. Oestreich), Wiley, Chichester, **2009**, pp 259–279.

[2] a) L.-C. Kao, F. G. Stakem, B. A. Patel, R. F. Heck, *J. Org. Chem.* **1982**, *47*, 1267–1277; b) T. Jeffery, *J. Chem. Soc. Chem. Commun.* **1991**, 324–325; c) T. Jeffery, *Tetrahedron Lett.* **1991**, *32*, 2121–2124; d) E. Bernocchi, S. Cacchi, P. G. Ciattini, E. Morera, G. Ortar, *Tetrahedron Lett.* **1992**, *33*, 3073–3076; e) T. Jeffery, *Tetrahedron Lett.* **1993**, *34*, 1133–1136; f) S.-K. Kang, K.-Y. Jung, C.-H. Park, E.-Y. Namkoong, T.-H. Kim, *Tetrahedron Lett.* **1995**, *36*, 6287–6290; g) S.-K. Kang, H.-W. Lee, S.-B. Jang, T.-H. Kim, S.-J. Pyun, *J. Org. Chem.* **1996**, *61*, 2604–2605; h) J. M. Ndungu, K. K. Larson, R. Sarpong, *Org. Lett.* **2005**, *7*, 5845–5848.

[3] S. Jeong, X. Chen, P. G. Harran, *J. Org. Chem.* **1998**, *63*, 8640–8641.

[4] a) M. Oestreich, F. Sempere-Culler, A. B. Machotta, *Angew. Chem.* **2005**, *117*, 152–155; *Angew. Chem. Int. Ed.* **2005**, *44*, 149–152; b) M. Oestreich, F. Sempere-Culler, A. B. Machotta, *Synlett* **2006**, 2965–2968; c) A. B. Machotta, B. F. Straub, M. Oestreich, *J. Am. Chem. Soc.* **2007**, *129*, 13455–13463.

[5] Y. Lu, D.-H. Wang, K. M. Engle, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 5916–5921.

[6] For related directed C–H bond activation employing a silanol, see: a) M. Mewald, J. A. Schiffner, M. Oestreich, *Angew. Chem.* **2012**, *124*, 1797–1799; *Angew. Chem. Int. Ed.* **2012**, *51*, 1763–1765; b) C. Huang, N. Ghavtadze, B. Chattopadhyay, V. Gevorgyan, *J. Am. Chem. Soc.* **2011**, *133*, 17630–17633; c) C. Wang, G. He, *Chem. Eur. J.* **2011**, *17*, 14371–14374.

[7] For selected reviews of directing groups in C–H bond alkenylation, see: a) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem.* **2009**, *121*, 5196–5217; *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115; b) E. M. Ferreira, H. Zhang, B. M. Stoltz, in: *The Mizoroki–Heck Reaction*, (Ed.: M. Oestreich), Wiley, Chichester, **2009**, pp 345–382; c) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068–5083; d) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147–1169; e) J. L. Bras, J. Muzart, *Chem. Rev.* **2011**, *111*, 1170–1214; f) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215–1292; g) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780–1824; h) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788–802.

[8] For the use of MPAAs as ligands, see: a) B.-F. Shi, N. Maugel, Y.-H. Zhang, J.-Q. Yu, *Angew. Chem.* **2008**, *120*, 4960–4964; *Angew. Chem. Int. Ed.* **2008**, *47*, 4882–4886; b) B.-F. Shi, Y.-H. Zhang, J. K. Lam, D.-H. Wang, J.-Q. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 460–461; c) ref.[5]; d) Y. Lu, D. Leow, X. Wang, K. M. Engle, J.-Q. Yu, *Chem. Sci.* **2011**, *2*, 967–971; e) M. Wasa, K. M. Engle, D. W. Lin, E. J. Yoo, J.-Q. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 19598–19601; f) G. Li, D. Leow, L. Wan, J.-Q. Yu, *Angew. Chem.* **2013**, *125*, 1283–1285; *Angew. Chem. Int. Ed.* **2013**, *52*, 1245–1247; g) G.-J. Cheng, Y.-F. Yang, P. Liu, P. Chen, T.-Y. Sun, G. Li, X. Zhang, K. N. Houk, J.-Q. Yu, Y.-D. Wu, *J. Am. Chem. Soc.* **2014**, *136*, 894–897.

[9] For leading references, see: a) A. Studer, F. Schleth, *Synlett* **2005**, 3033–3041; b) R. W. Hoffmann, *Synthesis* **2004**, 2075–2090.

[10] Li_2CO_3 is not soluble in DCE, and the reaction mixture is not homogeneous. An increased amount of solid Li_2CO_3 still seems to be beneficial as reflected in a higher isolated yield (52% as opposed to 42%).

[11] For a review of C–H bond functionalization of indoles, see: G. Broggini, E. M. Beccalli, A. Fasana, S. Gazzola, *Beilstein J. Org. Chem.* **2012**, *8*, 1730–1746.

[12] For oxidative palladium(II)-catalyzed intramolecular couplings of electron-rich arenes and hetarenes, see: a) E. M. Ferreira, B. M. Stoltz, *J. Am. Chem. Soc.* **2003**, *125*, 9578–9579; b) G. Abbiati, E. M. Beccalli, G. Broggini, C. Zoni, *J. Org. Chem.* **2003**, *68*, 7625–7628; c) H. Zhang, E. M. Ferreira, B. M. Stoltz, *Angew. Chem.* **2004**, *116*, 6270–6274; *Angew. Chem. Int. Ed.* **2004**, *43*, 6144–6148; d) E. M. Beck, N. P. Grimster, R. Hatley, M. J. Gaunt, *J. Am. Chem. Soc.* **2006**, *128*, 2528–2529; e) A. Kong, X. Han, X. Lu, *Org. Lett.* **2006**, *8*, 1339–1342; f) E. M. Ferreira, H. Zhang, B. M. Stoltz, *Tetrahedron* **2008**, *64*, 5987–6001; g) X. Han, X. Lu, *Org. Lett.* **2009**, *11*, 2381–2384; h) S. R. Kandukuri, J. A. Schiffner, M. Oestreich, *Angew. Chem.* **2012**, *124*, 1291–1295; *Angew. Chem. Int. Ed.* **2012**, *51*, 1265–1269.

[13] The fact that the OMe group is not acting as a directing group is remarkable as there are examples of ether-directed palladium-catalyzed C–H bond activation: a) Á. Iglesias, R. Álvarez, Á. R. de Lera, K. Muñiz, *Angew. Chem.* **2012**, *124*, 2268–2271; *Angew. Chem. Int. Ed.* **2012**, *51*, 2225–2228; b) ref.[8f]

[14] For a related carbazole formation, see: ref.[12e]

[15] a) J. A. Schiffner, A. B. Machotta, M. Oestreich, *Synlett* **2008**, 2271–2274; b) J. A. Schiffner, T. H. Wöste, M. Oestreich, *Eur. J. Org. Chem.* **2010**, 174–182.

[16] We are not aware of another example of an intramolecular C-2 alkenylation of an indole where an existing stereocenter induces reasonable diastereoselectivity in the construction of a quaternary carbon atom: ref.[12a]